

II. Amendments to the Claims

Claims 1-23. Canceled without prejudice.

24. (New) An orally administrable pharmaceutical composition comprising a therapeutically effective amount of an immediate release formulation comprising a (-) chiral compound enantiomer or a pharmaceutically acceptable salt thereof; and a controlled release formulation comprising a (+) chiral compound enantiomer or a pharmaceutically acceptable salt thereof and a heteropolysaccharide and polysaccharide gum excipient.

25. (New) The composition of claim 24, wherein the ratio of the heteropolysaccharide and polysaccharide gum excipient to (+) chiral compound enantiomer or pharmaceutically acceptable salt thereof is between about 1:3 to 3:1.

26. (New) The composition of claim 24, wherein the heteropolysaccharide and polysaccharide gum excipient comprises locust bean gum and xanthan gum.

27. (New) The composition of claim 24, wherein the controlled release formulation comprises a (+) chiral compound enantiomer or a pharmaceutically acceptable salt thereof and a controlled release delivery system comprising 25% locust bean gum, 25% xanthan gum, 35% dextrose, 10% calcium sulfate, and 5% ethylcellulose.

28. (New) The composition of claim 24, wherein the controlled release formulation comprises a (+) chiral compound enantiomer or a pharmaceutically acceptable salt thereof and a controlled release delivery system comprising 15% locust bean gum, 15% xanthan gum, 60% dextrose, and 10% calcium sulfate.

29. (New) The composition of claim 24, wherein the composition is a bi-layered tablet.

30. (New) The composition of claim 24, wherein the compound of the (+) and (-) chiral compound enantiomers is selected from the group consisting of warfarin, tramadol, mianserin, carvedilol, citalopram, dobutamine, aminoglutethimide, alfuzosin, celiprolol, cisapride, disopyramide, fenoldopam, flecainide, hydroxychloroquine, ifosfamide, labetolol, mexiletine, propafenone, tegafur, terazosin, thioctic acid, thiopental, and zacopride.

31. (New) The composition of claim 24, wherein, when measured by the USP type II dissolution method, the *in vitro* dissolution rate for the controlled release (CR) formulation and the immediate release (IR) formulation are:

Response and Amendment under 37 C.F.R. § 1.111

Application No. 09/970,020

Page 3 of 11

Time (hours)	% CR Release	% IR Release
0	0%	0%
0.3	0-60 %	20-100 %
0.5	0-65 %	20-100 %
1.0	5-70 %	25-100 %
2.0	5-75 %	25-100 %
4.0	10-80 %	30-100 %
6.0	10-100 %	30-100 %
8.0	20-100 %	40-100 %
10.0	25-100 %	45-100 %
12.0	25-100 %	45-100 %
18.0	35-100 %	50-100 %
24.0	35-100 %	50-100 %.

ai
32. (New) The composition of claim 24, wherein the (+) chiral compound enantiomer and the (-) chiral compound enantiomer are present in the composition at different mass quantities.

33. (New) The composition of claim 24, wherein the (+) chiral compound enantiomer and the (-) chiral compound enantiomer are present in the composition at a percent ratio selected from the following table:

(+) enantiomer	(-) enantiomer
2	1
3	1
4	1
5	1
10	1
1	2
1	3
1	4
1	5

1

10.

34. (New) The composition of claim 24, wherein about 90% of the (+) chiral compound enantiomer and about 90% of the (-) chiral compound enantiomer are released within about 12 hours of administration.

35. (New) The composition of claim 24, wherein when administered to a patient, the pharmaceutical composition provides the following percent of maximum (+) and (-) chiral compound enantiomer plasma concentrations:

Time (hours)	(+) Enantiomer	(-) Enantiomer
0	0%	0%
0.3	0-60 %	0-100 %
0.5	0-65 %	0-100 %
1.0	5-70 %	25-100 %
2.0	5-75 %	25-100 %
4.0	10-80 %	30-100 %
6.0	20-100 %	30-100 %
8.0	20-100 %	20-100 %
10.0	20-100 %	20-100 %
12.0	10-100 %	0-90 %
18.0	0-80 %	0-80 %
24.0	0-80 %	0-80 %.

36. (New) The composition of claim 24, wherein, when administered to a patient, the pharmaceutical composition provides the following percent of maximum (+) and (-) chiral drug enantiomer plasma concentrations:

Time (hours)	(+) Enantiomer	(-) Enantiomer
0	0%	0%
0.3	0-40 %	0-100 %
0.5	0-45 %	0-100 %
1.0	5-50 %	25-100 %
2.0	5-55 %	25-100 %
4.0	10-80 %	30-100 %

6.0	20-100 %	30-100 %
8.0	20-100 %	20-100 %
10.0	10-100 %	20-100 %
12.0	0-80 %	10-90 %
18.0	0-80 %	0-80 %
24.0	0-80 %	0-80 %.

37. (New) The composition of claim 24, wherein the compound of the (+) and (-) chiral compound enantiomers is tramadol.

38. (New) The composition of claim 37, wherein the (+) tramadol enantiomer and the (-) tramadol enantiomer are present in the composition at a percent ratio of 3:1.

39. (New) The composition of claim 37, wherein the (+) tramadol enantiomer and the (-) tramadol enantiomer are present in the composition at a percent ratio of 2:1.

40. (New) An orally administrable pharmaceutical composition comprising a therapeutically effective amount of an immediate release formulation comprising a (+) chiral compound enantiomer or a pharmaceutically acceptable salt thereof; and a controlled release formulation comprising a (-) chiral compound enantiomer or a pharmaceutically acceptable salt thereof and a heteropolysaccharide and polysaccharide gum excipient.

41. (New) The composition of claim 40, wherein the ratio of the heteropolysaccharide and polysaccharide gum excipient to (-) chiral compound enantiomer or pharmaceutically acceptable salt thereof is between about 1:3 to 3:1.

42. (New) The composition of claim 40, wherein the heteropolysaccharide and polysaccharide gum excipient comprises locust bean gum and xanthan gum.

43. (New) The composition of claim 40, wherein the controlled release formulation comprises a (-) chiral compound enantiomer or a pharmaceutically acceptable salt thereof and a controlled release delivery system comprising 25% locust bean gum, 25% xanthan gum, 35% dextrose, 10% calcium sulfate, and 5% ethylcellulose.

44. (New) The composition of claim 40, wherein the controlled release formulation comprises a (-) chiral compound enantiomer or a pharmaceutically acceptable salt thereof and a controlled release delivery system comprising 15% locust bean gum, 15% xanthan gum, 60% dextrose, and 10% calcium sulfate.

45. (New) The composition of claim 40, wherein the composition is a bi-layered tablet.

46. (New) The composition of claim 40, wherein the compound of the (+) and (-) chiral compound enantiomers is selected from the group consisting of warfarin, tramadol, mianserin, carvedilol, citalopram, dobutamine, aminoglutethimide, alfuzosin, celiprolol, cisapride, disopyramide, fenoldopam, flecainide, hydroxychloroquine, ifosfamide, labetolol, mexiletine, propafenone, tegafur, terazosin, thiocetic acid, thiopental, and zacopride.

47. (New) The composition of claim 40, wherein, when measured by the USP type II dissolution method, the *in vitro* dissolution rate for the controlled release (CR) formulation and the immediate release (IR) formulation are:

Time (hours)	% CR Release	% IR Release
0	0%	0%
0.3	0-60 %	20-100 %
0.5	0-65 %	20-100 %
1.0	5-70 %	25-100 %
2.0	5-75 %	25-100 %
4.0	10-80 %	30-100 %
6.0	10-100 %	30-100 %
8.0	20-100 %	40-100 %
10.0	25-100 %	45-100 %
12.0	25-100 %	45-100 %
18.0	35-100 %	50-100 %
24.0	35-100 %	50-100 %.

48. (New) The composition of claim 40, wherein the (+) chiral compound enantiomer and the (-) chiral compound enantiomer are present in the composition at different mass quantities.

49. (New) The composition of claim 40, wherein the (+) chiral compound enantiomer and the (-) chiral compound enantiomer are present in the composition at a percent ratio selected from the following table:

(+) enantiomer	(-) enantiomer
2	1
3	1
4	1
5	1
10	1
1	2
1	3
1	4
1	5
1	10.

A 50. (New) The composition of claim 40, wherein about 90% of the (+) chiral compound enantiomer and about 90% of the (-) chiral compound enantiomer are released within about 12 hours of administration.

51. (New) The composition of claim 40, wherein when administered to a patient, the pharmaceutical composition provides the following percent of maximum (+) and (-) chiral compound enantiomer plasma concentrations:

Time (hours)	(+) Enantiomer	(-) Enantiomer
0	0%	0%
0.3	0-60 %	0-100 %
0.5	0-65 %	0-100 %
1.0	5-70 %	25-100 %
2.0	5-75 %	25-100 %
4.0	10-80 %	30-100 %
6.0	20-100 %	30-100 %
8.0	20-100 %	20-100 %
10.0	20-100 %	20-100 %
12.0	10-100 %	0-90 %
18.0	0-80 %	0-80 %
24.0	0-80 %	0-80 %.

52. (New) The composition of claim 40, wherein, when administered to a patient, the pharmaceutical composition provides the following percent of maximum (+) and (-) chiral drug enantiomer plasma concentrations:

Time (hours)	(+) Enantiomer	(-) Enantiomer
0	0%	0%
0.3	0-40 %	0-100 %
0.5	0-45 %	0-100 %
1.0	5-50 %	25-100 %
2.0	5-55 %	25-100 %
4.0	10-80 %	30-100 %
6.0	20-100 %	30-100 %
8.0	20-100 %	20-100 %
10.0	10-100 %	20-100 %
12.0	0-80 %	10-90 %
18.0	0-80 %	0-80 %
24.0	0-80 %	0-80 %.

53. (New) The composition of claim 40, wherein the compound is tramadol.

54. (New) A bi-layered, orally administrable tablet comprising:

(a) a controlled release formulation comprising about 5.4% by weight (+) tramadol or a pharmaceutically acceptable salt thereof; about 37.7% by weight of a controlled release delivery system; about 16.2% by weight silicified microcrystalline cellulose; and about 0.6% by weight magnesium stearate; wherein the controlled release delivery system comprises 25% locust bean gum, 25% xanthan gum, 35% dextrose, 10% calcium sulfate, and 5% ethylcellulose; and

(b) an immediate release formulation comprising about 16.2% by weight (-) tramadol or a pharmaceutically acceptable salt thereof; about 10.8% by weight silicified microcrystalline cellulose; about 10.8% lactose fast flow; about 2.2% sodium starch glycolate and about 0.3 % by weight magnesium stearate;

wherein the % by weight is based on the weight of the bi-layered, orally administrable tablet.